Chapter

Managing Polypharmacy and Deprescribing in Elderly

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Abstract

The increase in the number of medications used may result many negative consequences for patients and health system. Elderly patients are more likely to encounter these health problems associated with polypharmacy. Deprescribing, the process of tapering, withdrawing, discontinuing, or stopping medications, is important in reducing polypharmacy, adverse drug effects, inappropriate or ineffective medication use, and costs. Deprescribing in elderly patients in accordance with the evidence based guidelines has many positive outcomes in older people such as decrease in the risk of falls, improvement in cognition, and improvement in patients' global health status. Therefore, each visit of an elderly patient should be considered as an opportunity to evaluate the unnecessary use or harms of the prescribed or nonprescribed medications. Clinicians should decide to deprescription process by individualized care goals in line with current guidelines. Beers Criteria, STOPP/START and The Medication Appropriateness Index-MAI can be used to assit clinicians to identify unnecessary or potentially inappropriate drugs and reduce the number of medications in older patients. But, a balance is required between over and under prescribing. In conclusion, prevention of polypharmacy and withdrawing unneccesary and inappropriate medications may be the best clinical decision for family physicians who follow the elderly in primary care.

Keywords: polypharmacy, deprescription, elderly, older adults, aging, drug use, advers drug events, primary care

1. Introduction

Although lacking a consensus definition, the concurrent use of two or more medications is described polypharmacy [1]. However, in many researches investigating the use of multiple medications and their effects, the concurrent use of 5 or more drugs is defined as "polypharmacy" [2–4]. The concurrent use of 2 or 3 medications does not cause a significant problem if they are chosen correctly, but the use of 4 or more medications carries a significant risk. Although polypharmacy is seen in all age groups, it is more common with increasing age. Nearly half of the older people use at least 1 drug even though it is not necessary [5, 6]. One of the most important causes for the increase in the number of medications used in the elderly is the coexistence of more than one chronic disease.

2. Polypharmacy in elderly

Increase in the number of medications used may cause many health problems. As the metabolism and elimination of drugs will be affected by the decrease in kidney and liver functions with increasing age, the older people are more susceptible to the negative effects of polypharmacy. In addition, with increasing age, the onset of amnesia, decreased visual acuity, and the onset of physical disabilities cause the elderly, who already use many drugs, to make mistakes in the use of drugs. As a result, the elderly are more likely to encounter many health problems caused by the use of multiple drugs. Therefore, polypharmacy is accepted as one of the geriatric syndromes.

Apart from increasing age and the presence of chronic disease, other risk factors for polypharmacy are listed below [7, 8]:

- Follow-up of patients by more than one physician and lack of communication between physicians
- Patients' drug expectations for their illness
- Medical guidelines specific to diseases, not to patients
- Pharmaceutical advertisements
- Recent hospitalization
- Over-the-counter drug sales
- Prescribing medication for symptoms rather than diagnosis
- Failure to adequately explain the medication changes to the patients by the doctors
- Residing in long-term care facilities
- Prescription cascade (addition of new medications to counter adverse drug reactions or drug side effects. For example, addition of an antitussive agent to relieve cough caused by angiotensin converting enzyme inhibitors, or addition of an antihypertensive due to increased blood pressure with NSAID use.

The increase in the number of medications used may result many negative consequences for patients and health system. For example, overall, 30% of hospital admissions are related in some way to medications in people aged over 65 years and half of these could be prevented [9]. Also, with increasing age, compliance to drug usage declines due to increase in the number of the drugs used, the beginning of memory loss, weakness of vision and the onset of physical incapabilities. The most common health problems reported in the elderly people associated with polypharmacy are listed below [10–15]:

- Increase risk of:
    - Drug interactions
    - Advers drug events

- Morbidity and mortality
- Physical and cognitive dysfunction
- Falls and associated harms (hip fracture, etc)
- Prescribing cascade

- Increase in use of the health care system and hospitalizations
- Decreased compliance to medication use
- Increased treatment cost
- Increased need of residing in long-term care facilities

As can be seen above, most of the problems caused by polypharmacy can be prevented. Visits for prescribing the medications used regularly, health maintanece and control visits are the convenient opportunities for physicians to evaluate drug interactions. In addition, while making a differential diagnosis for a new complaint or symptom, polypharmacy and drug interactions, should be evaluated and kept in mind that changes in the patient's condition may be associated with drug interactions or an adverse effect of a medication.

Although polypharmacy is referred to prescribed medications, the number of over-the-counter and herbal/dietary supplements used should be also considered. It should be noted that beside the all medications used by the patient, over-the-counter drugs with dietary or herbal supplements should be evaluated in terms of interactions. For example, garlic or *Ginkgo biloba* extract taken with warfarin may cause an increased risk of bleeding. St. John's wort taken with atorvastatin or diltiazem, may increase the advers effects of atorvastatin or diltiazem in older adults [16, 17].

Even not recommended by a physician, elderly people self-medicate more than the other age groups. This leads to an increased risk of adverse events and side effects. For example, the use of non-steroidal anti-inflammatory drugs, which are used common nonprescription, may lead to hypertension, decreased effect of the antihypertensives or a gastrointestinal bleeding.

There are many web-based applications developed for the physicians to control drug interactions. The addresses of some free applications that can be easily used on smartphones and tablets are listed below:

- http://www.drugs.com/drug_interactions.html
- http://reference.medscape.com/drug-interactionchecker?cid=med
- http://www.webmd.com/interaction-checker
- http://www.micromedex.com
- https://online.epocrates.com/interaction-check
- http://cpref.goldstandard.com/inter.asp?r=8084

Probably most of the medications used by the patients were prescribed and clinically indicated. However, some medications may be unnecessary or cause harm

over time due to physiological changes occur with aging or added health problems. These physiological changes that occur with aging affect the sensitivity of drugs mainly by causing changes in the pharmacokinetics of the drug. Pharmacodynamic changes also play a role, although to a lesser extent. The changes in the number and sensitivity of the receptors due to aging or some diseases that occur with aging, and the change of post-receptor events are the main reasons for the changes in pharmacodynamic responses of the medications. In general, these changes cause the effect of the drug to occur more or less and the emergence of drug toxicity and adverse drug reactions. Because of all these changes, the beneficial effects of drug use and the potential harmful effects of drug use should be evaluated together. The decrease in body functions, which occurs with aging is not the same in people of the same age. Therefore, the concept of "*patient centered assessment*" becomes even more important in the older age groups. Avoiding over-prescription and inappropriate drugs in elderly patients is the other important point in preventing adverse health problems caused by polypharmacy and changes due to aging. There are a few tools can be used to assit clinicians to identify unnecessary or potentially inappropriate drugs for older patients. Beers Criteria, Screening Tool of Older Person's Potentially Inappropriate Prescriptions (STOPP), Screening Tool to Alert to Right Treatment (START) and The Medication Appropriateness Index-MAI are some of them [18–20]. These tools allow the comparison of the patient's medications in terms of duplications, interactions, and potencially inappropriateness and to check for medication adjustments required for certain disease states, such as renal impairment.

Another problem encountered with the polypharmacy in the elderly is the use of narrow therapeutic index drugs. As a result of interaction of these drugs with other drugs the therapeutic dose can be easily increased to the toxic dose due to reduction in metabolism, increase in absorption or decrease in elimination. So, the medications with narrow therapeutic index may cause death even use in therapeutic doses. Small changes in the dosage of narrow therapeutic index drugs can lead to significant changes in pharmacodynamic response, particularly in elderly patients with comorbidities or using multiple medications. Therefore, recognizing the narrow therapeutic index drugs is very important issue in terms of preventing serious problems. Narrow therapeutic index drugs commonly used are shown in **Table 1**.

In the light of these information, each visit of an elderly patient should be considered as an opportunity to evaluate the unnecessary use or harms of the prescribed or nonprescribed medications. Studies showed that reducing the number of medications has many positive outcomes in older people such as decrease in the risk of falls, improvement in cognition, and improvement in patients' global health

- Amiodarone
- Carbamazepin
- Cyclosporine
- Digoxin
- Gentamicin
- Levothyoxine
- Lithium carbonate
- Morfin
- Phenytoin
- Tacrolimus
- Theophylline
- Valproic acide
- Warfarin

Table 1.
Common narrow therapeutic ındex drugs.

status [21–23]. Moreover, approxymately, over half of the people over 70 years of age medicines could be discontinued [24].

In some cases, it is necessary to use multiple drugs for therapeutic purposes at once. For example, concomitant use of aspirin, beta-blockers, ACE inhibitors and lipid-lowering drugs is inevitable in cardiovascular diseases. For this reason, what needs to be done is to try to keep the number of drugs as few as possible by making a risk–benefit assessment by considering the personal treatment goals [25, 26].

In addition to the unnecessary and excessive use of drugs in the elderly, another important problem is that some drugs are not prescribed by physicians or are not used by patients, even though they are necessary. For example, it has been reported that only half of the patients take an anticoagulant in atrial fibrillation, although the guidelines suggest. It has also been reported that inhaled anticholinergic bronchodilators in COPD, SSRIs in depression, ACE inhibitors in the presence of diabetes mellitus and hypertension are not prescribed although necessary [27]. The other medications that are often underprescribed in the elderly include those used to Alzheimer disease, pain (eg, opioids), heart failure, post-MI (β-blockers), glaucoma, and incontinence. In addition to the medications, vaccines are not prescribed as recommended.

3. Deprescription process

Deprescribing, the process of tapering, withdrawing, discontinuing, or stopping medications, is important in reducing polypharmacy, adverse drug effects, inappropriate or ineffective medication use, and costs [28]. The first step in deprescription is the identifing the patients with risk. To identifying the patients with risk, a comprehensive geriatric assessment should be necessery. Comprehensive geriatric assessment is a systematic evaluation of older people by a multidisciplinary health professionals to determine the medical, psychological and functional capabilities and develop a coordinated and integrated personalized follow up plan. Comprehensive geriatric assessment of the elderly patient in primary care should include multimorbidity, cognitive changes, functional status changes, frailty, risk of falling, medication nonadherence, polypharmacy, transitions in care setting, unexplained weight loss, and family concerns for safety [29]. Although comprehensive geriatric assessment expected to be performed by a multidisciplinary health professionals, family physicians have a central role in comprehensive geriatric assessment and coordinating the care. Comprehensive geriatric assessment can be performed in over time with regularly scheduled visits in primary care. During each visit, it should be targeted at least one domain and evaluation of polypharmacy risk and polypharmacy related problems prioritized. Periodic evaluation of a patient's drug regimen and risk of polypharmacy and adverse drug events is an essential component of comprehensive geriatric assessment. Patients need to be specifically told to bring all of the over-the-counter products, ointments, vitamins, ophthalmic preparations, or herbal medicines, used by them to the visit.

It should be aimed to reduce the number of drugs, particularly in those use 7 or more drugs, a history of adverse drug reactions or falls, develope confusion or lethargy as a new symptom, worsen general health status, transfered to nursing homes, have multiple care providers or cared by more than one institutions. Anticipation of polypharmacy and inappropriate drug use is a part of deprescription process. Approximately one-fifth of the drugs used in elderly people are inappropriate drugs [30].

To reduce the number of medications used in older patients, Beers Criteria, Screening Tool of Older Person's Potentially Inappropriate Prescriptions (STOPP),

Screening Tool to Alert to Right Treatment (START) and The Medication Appropriateness Index-MAI can be used by the physicians [18–20]. The STOPP/START guideline contributes to the recognition of potentially inappropriate drugs for use in elderly patients and to drug selection in common diseases with evidence-based recommendations. The Beers Criteria is a guide to identify the inappropriate drugs that should be avoided in the elderly. The criteria include three categories: those that should always be avoided (regardless of disease or condition (eg, diphenhidramine, benzodiazepines); those that are potentially inappropriate in older adults with particular health conditions or syndromes; and those that should be used with caution (eg, carbamazepines, SSRIs) [19]. Medical Appropriateness Index, contributes to the evaluation of each medications in terms of indication, efficacy, appropriate dose and correct use, drug interactions, presence of medications with similar effect, appropriate treatment duration and cost [20].

It can be predicted that polypharmacy and unnecessary drugs may be used by the patients recently discharged from the hospital. It is known that medications used temporarily during hospitalization are also continued to use after discharge by the patients. Therefore, after discharge from the hospital, medications used by the patients should be reviewed. Additionally, increasing age, female gender, higher levels of education, cognitive dysfunction, general poor health, having cardiovascular disease, hypertension, asthma, diabetes or using high-risk drugs (antithrombotic agents, insulin, oral hypoglycaemic agents, cardiovascular and central nervous system drugs, anticolinergics) are the risks for polypharmacy and adverse drug events.

After the risk identification, the physician should prepare the patient and their closers to deprescribing. Asking the elderly and caregivers, which medications they prefer to use, and getting their opinion will make it easier for the physician. Because the passion of the elderly to some drugs can be an obstacle in the process of deprescribing, and the insistent attitude of the physician to discontinue the drug may reduce the trust to the doctor. Moreover, learning the patients' and caregivers' preferences are the first step of shared decision making process, that be very important in patient centered approachment in primary care.

Prioritization of the medicines to cease or doses to reduce is the second step of deprescription [31, 32]. For this, it should be checked the medications in terms of there is still a valid indication and benefit, presence of adverse drug reactions or new symptoms and risky drugs eg. anticholinergic and sedating drugs.

If there is a medication that is not preferred by the patient among the medications considered for discontinuation, deprescription can be started by discontinuing this medication.

If any adverse drug reaction or new symptom are suspected, the suspected drug should be discontinued first, and the next target medication to discotinue should be anticholinergic and sadative drugs. Because elderly patients are particularly susceptible of anticholinergic and sedating drugs advers effects. Adverse effects associated with anticholinergic use in older adults include memory impairment, confusion, hallucinations, dry mouth, blurred vision, constipation, nausea, urinary retention, impaired sweating, and tachycardia [33, 34]. Moreover, it was reported an association between anticholinergic use and risk of community acquired pneumonia [35]. Presence of these symptoms should be a warning to the physician. Some examples of anticholinergic drugs are shown in **Table 2**.

Discontinuation of the drugs with similar effects is another step in reducing the number of drugs. Then, the presence of drugs that can be used in combination among the drugs used should be reviewed, and if possible, the number of drugs should be reduced by prescribing the medications in combination.

- Anti-arrhythmic drugs
  - Procainamide
  - Disopyramide
- Antihistamines
  - Chlorphenamine
  - Diphenhydramine
  - Cyproheptadine
  - Hydroxyzine
  - Promethazine
- Antidepressants
  - Amitriptyline
  - Dosulepin
  - Doxepin
  - Clomipramine
  - Imipramine
  - Nortriptyline
- Antipsychotics
  - Chlorpromazine
  - Clozapine
  - Olanzapine
- Bronchodilators
  - Ipratropium
  - Tiotropium
- Drugs for urinary frequency, enuresis and incontinence
  - Flavoxate
  - Oxybutynin
  - Tolterodine
  - Darifenacin
  - Trospium
- Antiparkinson drugs
  - Trihexyphenidyl (benzhexol)
  - Orphenadrine
  - Amantadine
- Mydriatics and cycloplegics
  - Atropine
  - Cyclopentolate
  - Tropicamide
- Antispasmodics
  - Dicycloverine
  - Hyoscine butylbromide
- Antiemetics
  - Hyoscine hydrobromide
  - Prochlorperazine
- Skeletal muscle relaxants
  - Methocarbamol
  - Antidiarrhoeals
  - Diphenoxylate

Table 2.
Anticholinergic drugs.

Physicians should assess whether treatment goals have changed for the patient at each visit. In updated guidelines, treatment goals may change based on new evidence or depending on the patient's age or other intervening disease. For example, after recognizing that strict targeting for hemoglobin A1c and blood pressure values was harmful in the elderly, the guidelines were updated on this issue [36, 37]. In addition to goals of care, the patients' life expectancy also considered in deprescription process. The patient's life expectancy may have been decrease by an intervening cancer or other serious illness. In this case, some medications that are expected to show their effects in long term (eg statins), can be discontinued.

• Risk identification and anticipation
• Defining inappropriate or unnecessary medicine use
• Preparation of patient and their closers to deprescription
• Learning patient and caregivers preferences
• Prioritization of the medicines to cease or doses to reduce
• Checking valid indication and benefit of the medications
• Checking adverse drug reactions or new symptoms
• Identification anticholinergic and sedating drug use
• Identification of medications with similar effects
• Reviewing the presence of drugs that can be used in combination
• Assessing whether treatment goals have changed
• Considering non-pharmacologic options

Table 3.
The steps of deprescription.

Clinicians should decide to discontinuation process by individualized treatment goals in line with current guidelines.

It is known that non-pharmacological treatments are even more effective than drug treatment in several chronic diseases. Therefore, while prescribing, non-pharmacologic treatment options should always be considered first [26]. If the patient can apply non-pharmacologic options, it will be easier to reduce the number of drugs. For example, in many patients, hypertension can be controlled only by sodium restriction or weight loss. In diabetes mellitus patients the number and dose of the medications can be reduced by low glycemic index diet and exercise.

The steps of deprescription process was shown in **Table 3**.

If it is not possible to cease of medications, it should be considered whether it is possible to reduce their dose. Because, many adverse drug reactions are dose-related. While prescribing it is important to use the minimal dose required to obtain clinical benefit.

3.1 Points to consider when reducing the number of medications

- A comprehensive geriatric assessment should be necessery to detect the risk of polypharmacy, polypharmacy related problems, possibility to reduce the number of medications and anticipate the consequences of withdrawal. Although consern of withdrawal reactions may be a barrier to deprescription, withdrawal reactions are seen rare when discontinuation is carried slowly and carefully [38].

- While reducing the number of drugs, it is very important that some drugs should be discontinued by tapering over time. Anticonvulsants, benzodiazepines, corticosteroids, antidepressants, beta blockers, levodopa, opiates, proton pump inhibitors, and gabapentin are the examples of drugs that should not be stopped abruptly. Abrupt discontinuation of these drugs may cause withdrawal syndrome and a rebound effect.

- Only stop or reduce one medicine at a time.

- Possible problems that may occur in case of discontinuation of the drug should be anticipated.

- Drug interactions should also be considered while reducing the number of drugs. For example, when using warfarin with omeprazole, discontinuation of

omeprazole, the INR may decrease because omeprazole had been inhibiting the metabolism of warfarin.

- In cases where it cannot be decided which medication should be discontinued, a collaboration with other physicians following the patient should be established.

- The necessity of drug discontinuation should be explained to the patient and their closers with an appropriate communication language.

- Effort should be made to improve communication in transition of the patients between health care centers or caregivers. Sharing the medication lists used by the patients or planned to withdrawal, between health providers at the time of care transition may be help to prevent adverse drug events.

- After the drug is withdrawal, warning messages about the discontinuation of the medications should be given to the patients in writing, a follow-up appointment should be planned, and should be informed about when to consult a doctor [39].

- Patients and their closers should be informed about the monitoring of blood parameters that may change after drug withdrawal.

- While trying to prevent polypharmacy and polypharmacy-related problems in elderly patients and to reduce unnecessary and inappropriate drug use, care should be taken not to discontinue the drugs that the patient really needs. START criteria is developed to help the identify potential prescribing omissions in older patients can be used in this regard [18].

- If treatment is indicated, the current regimen with a higher probability of adverse effects can be replaced with a safer alternative medication. As an example, acetaminophen instead of NSAID.

4. Conclusion

The patient's condition and goals of care changed over time are the key principles to be considered in deprescription. A comprehensive geriatric assessment should be necessery to detect the risk of polypharmacy, polypharmacy related problems, possibility to reduce the number of medications and anticipate the consequences of withdrawal. Avoiding from over-prescribing and inappropriate medications in older patients is the key step to prevent negative health problems due to polypharmacy. It should be kept in mind that in addition to over-prescribing, under-prescribing appropriate medications is also of concern in older patients. Therefore, a balance is required between over- and under-prescribing.

It should be kept in mind that reducing the number of drugs in the elderly patients in accordance with the evidence based guidelines can be carried without any serious problems and this situation can improve the health parameters of the older patients. In conclusion, prevention of polypharmacy and withdrawing unneccesary and inappropriate medications may be the best clinical decision in older patients.

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